REVIEWER COMMENTS. This study was chosen for review because of the potential frequency of this problem in patients with recurrent infection. This descriptive, retrospective study had a very mixed population, and some of the patients included would not meet a rigorous definition of SPADS (some with autoimmune disease, poor response to protein antigens). The definition of an abnormal response to pneumococcal vaccination was not well established. The practice parameter for the diagnosis and management of primary immunodeficiency defines response to pneumococcal polysaccharide vaccine as postimmunization antibody concentration of >1.3 μg/mL or fourfold rise over baseline. Children younger than 2 years should not be given a diagnosis of SPADS, because they have a physiologic impairment of antibody production to unconjugated polysaccharide antigens. Prospective studies for a more specific definition and response to treatment are needed for patients with specific antibody deficiency and normal IgG levels.

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HUMAN IMMUNODEFICIENCY VIRUS

Immune Reconstitution Syndrome After Highly Active Antiretroviral Therapy in Human Immunodeficiency Virus-Infected Thai Children

PURPOSE OF THE STUDY. Immune reconstitution inflammatory syndrome (IRIS) is a clinical phenomenon characterized by paradoxical worsening of the clinical status of patients with HIV who receive highly active antiretroviral therapy. It is presumed that this is a result of improvement in cellular immune functions and secondary immunopathology in response to organisms that had not been recognized previously. This syndrome has been well described in adult patients. The purpose of this study was to describe IRIS after initiation of highly active antiretroviral therapy in HIV-infected children.

STUDY POPULATION AND METHODS. There were 153 HIV-infected children enrolled at initiation of antiretroviral therapy and then followed prospectively.

RESULTS. Of the 153 children, 29 (19%) experienced 32 episodes of IRIS. The median time of onset was 4 weeks after initiation of antiretroviral therapy. Fourteen episodes were caused by mycobacterial organisms, 7 by varicella-zoster virus, 7 by herpes simplex virus, 3 by Cryptococcus neoformans, and 1 by Guillain-Barré syndrome. In general, treatment was not interrupted, and only 2 patients were treated with short courses of corticosteroids. However, 3 patients died as a result of IRIS or its complications. It is important to note that patients who reactivated mycobacterial disease had substantially lower CD4+ T-cell counts at the time that their antiretroviral therapy was started, compared with patients who reactivated herpes viruses.

CONCLUSIONS. IRIS is common among HIV-infected children who initiated antiretroviral therapy in an advanced stage of HIV disease.

REVIEWER COMMENTS. Ideally, this type of experience will become less common as patients have access to antiretroviral therapy before profound immunosuppression. However, we had a recent experience with a nonadherent teenager who, after developing disseminated Mycobacterium avium complex, decided to take his medication; a serious IRIS picture developed with persistent high-grade fever, severe abdominal pain, and dramatic intraabdominal adenopathy. Symptoms resolved rapidly with initiation of corticosteroid therapy. The challenge in such patients is to balance the management of their underlying HIV disease, their complicating opportunistic infection, and their immunosuppression to allow for resolution of the infection, reconstitution of immune function, and reduction in the complexity of their treatment regimen.

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PD-1 Expression on HIV-Specific T Cells Is Associated With T-Cell Exhaustion and Disease Progression

Upregulation of PD-1 Expression on HIV-Specific CD8+ T Cells Leads to Reversible Immune Dysfunction

PURPOSE OF THE STUDIES. Recent evidence from a mouse model of chronic viral infection suggests a crucial role for the programmed death 1 (PD-1)/programmed death 1 ligand (PD-L1) signaling pathway in downregulating the functions of virus-specific CD8+ T cells. PD-1 is an inhibitory receptor that negatively regulates activated T cells, and it is markedly upregulated on the surface of “exhausted” virus-specific CD8+ T cells in mice. HIV similarly induces a virus-specific impairment of T-cell functions. The purpose of these 2 studies was to investigate the expression of PD-1 on HIV-specific T cell in patients infected with the virus.

STUDY POPULATION AND METHODS. Both studies evaluated subjects with HIV and healthy controls and compared PD-1
Immune Reconstitution Syndrome After Highly Active Antiretroviral Therapy in Human Immunodeficiency Virus-Infected Thai Children

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